

Serial No. 09/779,376
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REMARKS

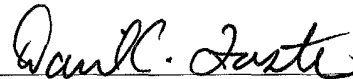
In response to the outstanding Restriction Requirement in this application, Applicants elect for further prosecution the claims of Group II, namely Claims 5, 9-16, 19-23, and 26, drawn to allele specific OLA and amplification with universal primers. This election is made without traverse. Please cancel, without prejudice, Claims 1-4, 6-8, 17-18, 24-25, and 27-29 as being drawn to non-elected inventions.

Support for the claim amendments can be found in the Claims, because the amendments merely corrected typographical errors and dependancy inconsistencies. No new matter has been added.

A copy of the currently pending claims is attached hereto as Appendix A, for the Examiner's convenience. A copy of the version showing changes made to the claims is attached hereto as Appendix B, for the Examiner's convenience.

Respectfully submitted,

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Appendix A
Pending claims

5. A method of determining the identification of a nucleotide at a detection position in a target sequence comprising a first target domain comprising said detection position and a second target domain adjacent to said detection position, wherein said method comprises:
- a) hybridizing a first ligation probe to said first target domain, said first ligation probe comprising:
 - i) an upstream universal priming site (UUP); and
 - ii) a first target-specific sequence; and
 - b) hybridizing a second ligation probe to said second target domain, said second ligation probe comprising:
 - i) a downstream universal priming site (DUP); and
 - ii) a second target-specific sequence comprising a first base at an interrogation position;
- wherein if said first base is perfectly complementary to said nucleotide at said detection position a ligation complex is formed and wherein at least one of said first and second ligation probes comprises an adapter sequence;
- c) removing non-hybridized first probes;
 - d) providing a ligase that ligates said first and second ligation probes to form a ligated probe;
 - e) amplifying said ligated probe to generate a plurality of amplicons;
 - f) contacting said amplicons with an array of capture probes; and
 - g) determining the nucleotide at said detection position.
9. (Amended) A method according to claim 5 or 26 wherein said removing comprises:
- a) enzymatically adding a binding ligand to said target sequence;
 - b) binding a hybridization complex comprising said target sequence comprising said binding ligand to a binding partner immobilized on a solid support;
 - c) washing away unhybridized probes; and
 - d) eluting said probe off said solid support.
10. (Amended) A method according to claim 5 or 26 wherein said removing is done using a double-stranded specific moiety.

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11. A method according to claim 10 wherein said double-stranded specific moiety is an intercalator attached to a support.
12. A method according to claim 9 wherein said support is a bead.
13. (Amended) A method according to claim 5 or 26 wherein said amplifying is done by:
 - a) hybridizing a first universal primer to said UUP;
 - b) providing a polymerase and dNTPs such that said first universal primer is extended;
 - c) hybridizing a second universal primer to said DUP;
 - d) providing a polymerase and dNTPs such that said second universal primer is extended; and
 - e) repeating steps a) through d).
14. (Amended) A method according to claim 5 or 26 wherein said array comprises:
 - a) a substrate with a patterned surface comprising discrete sites; and
 - b) a population of microspheres comprising at least a first subpopulation comprising a first capture probe and a second subpopulation comprising a second capture probe.
15. A method according to claim 14 wherein said discrete sites comprise wells.
16. A method according to claim 14 or 15 wherein said substrate comprises a fiber optic bundle.
19. (Amended) A method according to claim 5 or 26, further comprising providing a support on which the target sequence is immobilized.
20. A method according to claim 19, wherein said non-hybridized first probes are removed without removing said target sequence from said support.
21. (Amended) A method according to claim 5 or 26, further comprising attaching said target sequence to a support.
22. A method according to claim 21, wherein said target sequence is attached to said support by a method selected from the group consisting of labeling said target sequence with a functional attachment moiety, absorption of said target sequence on a charged support, direct chemical attachment of said target sequence to said support and photocrosslinking said target sequence to said support.

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23. (Amended) A method according to claim 5 or 26, wherein said support is selected from the group consisting of paper, plastic and tubes.

26. (Amended) A method of determining the identification of a nucleotide at a detection position in a target sequence comprising a first target domain comprising said detection position and a second target domain adjacent to said detection position, wherein said method comprises:

- a) providing a support on which the target sequence is immobilized;
- b) hybridizing a first ligation probe to said first target domain, said first ligation probe comprising:

- i) an upstream universal priming site (UUP); and
 - ii) a first target-specific sequence; and

- c) hybridizing a second ligation probe to said second target domain, said second ligation probe comprising:

- i) a downstream universal priming site (DUP); and
 - ii) a second target-specific sequence comprising a first base at an interrogation position;

wherein if said first base is perfectly complementary to said nucleotide at said detection position a ligation complex is formed and wherein at least one of said first and second ligation probes comprises an adapter sequence;

- d) removing non-hybridized first probes;

- e) providing a ligase that ligates said first and second ligation probes to form a ligated probe;

- f) amplifying said ligated probe to generate a plurality of amplicons;

- g) contacting said amplicons with an array of capture probes; and

- h) determining the nucleotide at said detection position.

Appendix B
Version showing changes made

5. A method of determining the identification of a nucleotide at a detection position in a target sequence comprising a first target domain comprising said detection position and a second target domain adjacent to said detection position, wherein said method comprises:
- a) hybridizing a first ligation probe to said first target domain, said first ligation probe comprising:
 - i) an upstream universal priming site (UUP); and
 - ii) a first target-specific sequence; and
 - b) hybridizing a second ligation probe to said second target domain, said second ligation probe comprising:
 - i) a downstream universal priming site (DUP); and
 - ii) a second target-specific sequence comprising a first base at an interrogation position;
- wherein if said first base is perfectly complementary to said nucleotide at said detection position a ligation complex is formed and wherein at least one of said first and second ligation probes comprises an adapter sequence;
- c) removing non-hybridized first probes;
 - d) providing a ligase that ligates said first and second ligation probes to form a ligated probe;
 - e) amplifying said ligated probe to generate a plurality of amplicons;
 - f) contacting said amplicons with an array of capture probes; and
 - g) determining the nucleotide at said detection position.
9. (Amended) A method according to claim [1, 4, 5, 6 or 8] 5 or 26 wherein said removing comprises:
- a) enzymatically adding a binding ligand to said target sequence;
 - b) binding a hybridization complex comprising said target sequence comprising said binding ligand to a binding partner immobilized on a solid support;
 - c) washing away unhybridized probes; and
 - d) eluting said probe off said solid support.
10. (Amended) A method according to claim [1, 4, 5, 6 or 8] 5 or 26 wherein said removing is done using a double-stranded specific moiety.

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11. A method according to claim 10 wherein said double-stranded specific moiety is an intercalator attached to a support.
12. A method according to claim 9 wherein said support is a bead.
13. (Amended) A method according to claim [1, 4, 5, 6 or 7] 5 or 26 wherein said amplifying is done by:
 - a) hybridizing a first universal primer to said UUP;
 - b) providing a polymerase and dNTPs such that said first universal primer is extended;
 - c) hybridizing a second universal primer to said DUP;
 - d) providing a polymerase and dNTPs such that said second universal primer is extended; and
 - e) repeating steps a) through d).
14. (Amended) A method according to claim [1, 4, 5, 6 or 7] 5 or 26 wherein said array comprises:
 - a) a substrate with a patterned surface comprising discrete sites; and
 - b) a population of microspheres comprising at least a first subpopulation comprising a first capture probe and a second subpopulation comprising a second capture probe.
15. A method according to claim 14 wherein said discrete sites comprise wells.
16. A method according to claim 14 or 15 wherein said substrate comprises a fiber optic bundle.
19. (Amended) A method according to claim [1, 4, 5, 6 or 7] 5 or 26, further comprising providing a support on which the target sequence is immobilized.
20. (Amended) A method according to claim 19, wherein said non-hybridized first probes are removed without removing said target sequence from said support.
21. (Amended) A method according to claim [1, 4, 5, 6 or 7] 5 or 26, further comprising attaching said target sequence to a support.
22. A method according to claim 21, wherein said target sequence is attached to said support by a method selected from the group consisting of labeling said target sequence with a functional attachment moiety, absorption of said target sequence on a charged support, direct

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chemical attachment of said target sequence to said support and photocrosslinking said target sequence to said support.

23. (Amended) A method according to claim [1, 4, 5, 6 or 7] 5 or 26, wherein said support is selected from the group consisting of paper, plastic and tubes.

26. (Amended) A method of determining the identification of a nucleotide at a detection position in a target sequence comprising a first target domain comprising said detection position and a second target domain adjacent to said detection position, wherein said method comprises:

- a) providing a support on which the target sequence is immobilized;
- b) hybridizing a first ligation probe to said first target domain, said first ligation probe comprising:

- i) an upstream universal priming site (UUP); and
- ii) a first target-specific sequence; and

- c) hybridizing a second ligation probe to said second target domain, said second ligation probe comprising:

- i) a downstream universal priming site (DUP); and
- [ii)] ii) a second target-specific sequence comprising a first base at an interrogation position;

wherein if said first base is perfectly complementary to said nucleotide at said detection position a ligation complex is formed and wherein at least one of said first and second ligation probes comprises an adapter sequence;

- d) removing non-hybridized first probes;
- e) providing a ligase that ligates said first and second ligation probes to form a ligated probe;

- f) amplifying said ligated probe to generate a plurality of amplicons;
- g) contacting said amplicons with an array of capture probes; and
- h) determining the nucleotide at said detection position.